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Tablet in Capsule Technology – Overview

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ABSTRACT

Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They are the most widely preferred form of medication both by pharmaceutical manufacturer as well as physicians and patients. Capsules are solid dosage forms in which drug is enclosed within either a hard or soft soluble shell. The shells are generally made up of gelatin. The capsules may be regarded as the container drug delivery system for powder and non-powder filling such as tablets, capsules and pellets. Tablet in capsule is a multifunctional and multiple unit system, which contains versatile mini-tablets in a hard gelatin capsule. It can be developed by preparing Rapid-release Mini-Tablets, Sustained-release Mini-Tablets, Pulsatile Mini-Tablets, and Delayed-onset Sustained-release Mini-Tablets, each with various lag times of release and encapsulating in a capsule. Biphasicdeliverysystemcanbeachievedinthisdosagef ormanditcanproducetherapidon set of release for those drugs that need prompt appearance of the rapeutic effect, followed by an extended release phase at a constant rate.MP formulations generally have a more reliable in-vivo dissolution performance when compared to a single unit dosage form, resulting in more uniform bioavailability and clinical effect. The rationale of mini tablets formulation is to accomplish several releases in one formulation by combining altered dose.

Keywords: Mini-tablets, Capsule, Multiple units, Tablet in capsule, Drug release.

I. INTRODUCTION

The most convenient and popular route of administration among all drug delivery routes is oral drug delivery. The main goal of any dosage form is to keep up the therapeutic amount of drug to the targeted site with minimum toxicity and side effects by providing loading and maintenance dose. Tablets are most widely used solid dosage form and there is always a possibility for improving the confines of tablets like delay in onset of action and difficulty in swallowing and improves patient compliance and have many advantages when compared with other dosage forms such as ease of transportation, production and application, accurate dosing, stability, and controlled release patterns were achieved [1-4].

The traditional solid dosage forms such as tablets and capsules considered as not proper due to swallowing difficulties in young children. Due to lack of its stability, dose accuracy, and dispensing faults, special attention is given to the progress of mini tablets to overcome these problems, with the aim to improve drug delivery for paediatrics. Mini tablets symbolize a new development in solid dosage form design and can use as a flexible drug delivery tool for single or composite of multiple units. Furthermore, mini tablets with well-controlled quality features could be a practical choice for administrating solid dosage forms of low potency drug substances as capsules or stick packs [5].

A capsule is an solid oral dosage form in which the active ingredients and diluents are contained in a two-piece hard shell, usually made of gelatin. Gelatin capsules are available in various sizes and colors. The double-zero size is the largest size for oral use in humans, although the zero size is more commonly used. The zero-size capsule has a capacity of 0.5 to 0.8 grams of powder depending on the density of the chemical being used. Hard-shell capsules consist of two pieces: the body and the cap. After the two pieces are separated, the body piece is filled with the dry powder ingredients and the cap is then replaced. The smallest capsule that will hold the ingredients can be chosen for the compound. When several ingredients are being inserted into the capsule, a powder that is near the average weight of all the ingredients can be chosen to determine the capsule size that will best accommodate the ingredients in a slightly packed form. If the amount of drug needed for a single dose is below the minimum weighable quantity, a diluent should be added. If the single dose is too large for a capsule that can reasonably be swallowed by the patient, a diluent can be added and the dose divided into two capsules [6].

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Advantages of Solid Oral Dosage Forms [7]

- They are the most stable dosage form with respect to their physical, chemical and microbiological attributes.
- Provide an accurate, stable dose with greatest precision and least content variability, easy to use, handle and to be carried by the patient.
- They are attractive and elegant in appearance.
- The manufacturing cost of tablets is low as compared to other dosage form and their manufacturing speed is also quite high.
- The packaging and shipping of tablets is comparatively easy and cheap.
- The unpleasant taste and od or of medicament(s) can be easily masked.
- The incompatibilities of medicament(s) and their deterioration due to environmental factors are less.
- They are more suitable for large scale production.
- Their identification is probably the easiest because of variety of shapes and colors.
- They are formulated with certain special release profile products such a senteric or delayed release products.
- They are the lightest and most compact dosage form.

Disadvantages of Solid Dosage Forms[7]

- Drugs that are amorphous in nature or have low density character are difficult to be compressed into tablet.
- Hygroscopic drugs are not suitable candidate for compressed tablets.
- Drugs having poor wetting properties, slow dissolution profile and high optimal gastro intestinal absorption are difficult or impossible to formulate as a tablet.
- Drugs having bitter taste and objection able odor require special treatment like coating or encapsulation which may increase their production cost.
- Some drugs which preferably get absorbed from the upper part of GIT may cause bio availability problem in tablet dosage form.
- Capsules cannot be used for extremely soluble materials such as potassium chloride, potassium bromide.
- Capsules cannot be used for highly efflorescent or deliquescent fill materials.

ORAL CONTROLLED RELEASE DRUG DELIVERY SYSTEMS (DDS)CAN BE CATEGORIZED IN TWO GROUPS [8]

1. Tablets and capsules which come under a class of single unit dosage forms (SUDF's). In a single unit dose, for example, matrix or tablet surrounded in diffusion membrane is a depot which releases drug throughout the passage of entire gastrointestinal (GI) tract without disintegrating. The empty core or shell was discharged. To keep a depot, effect the dose unit to be administered should be intact as dividing dosage form before administration would result in unintended rapid release.

2. Multiple unit dosage forms (MUDF's) such as granules, pellets, or mini tablets. A multiple unit's dose consists of several mini units, for example, pellets or mini tablets contained in a capsule or a tablet. These mini depots were dispersed and distributed throughout the GI tract with the disintegration of the tablet or capsule. The dose in (MUDF's) is divided into several subunits, each one containing the drug. The extent of the drug in each subunit and the functionality of the complete dose are directly correlated to the functionality of the specific subunits.

MINI TABLETS

The term "mini tablets" usually refers to compresses tablets with a smaller size than typical tablets. These are plain or blended tablets which are having a diameter ranging between 3 and 6 mm and less than that. Mini-tablets also called as oral granules because of its small diameter which is less-than 2.5 mm but the preparation and production of mini tablets mainly focused at their size range to take benefits of the potential flexibility in dosage form administration [9].

Mini tablets were produced with multiple punches using peculiar or rotary tablet press machines. Mini tablets are great substitutes for granules and pellets since they can easily produce and converted into a controlled DDS. Controlling drug release is a significant point of investigation in case of oral controlled drug release system [10].

Mini tablets helpful in reducing the intra and inter-subject variability and reproducible release profiles can be achieved. Preferably, the drug absorption is more in the upper part of small intestine for a drug to reach the small intestine and then it had to pass through stomach and the drug absorption depends on gastric emptying time. If the gastric emptying is too slow, it may get mix up

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with gastric contents or if it is fast drug may not absorb to the required level. These effects are more in the case of SUDFs because of their size, but in the case of mini tablets will not depend on gastric emptying and easily get distributed through pylorus. Hence, mini tablets are beneficial over the normal size tablets to lessen intra and inter-subject variability [11].

Advantages of the mini tablets [12]

• Their production is easy. It is an alternative to pellets and granules due to its reproducible production and dimensional similarity.
• Provides more uniform release kinetics. Thus, the risk of sudden increase in blood concentration is reduced.
• Formulation development is easy.
• İntra and inter individual variability is low. Because the size is too small, even if the pylorus is closed, it can pass to the intestine.
• They can be easily coated thanks to shape and size uniformity.
• The risk of local irritation is reduced because they spread throughout the gastrointestinal tract.
• Drug loading capacity is high.
• Setting the release profile is easy.
• Superiority to pellets
• Pellets are usually bead-like structures filled into capsules or compressed in tablets.
• Pellets are produced by fluid bed granulation or extrusion-spheronization methods, while mini tablets are produced by simple tablet production methods. This saves time and money.
• The absence of solvent use in production increases the stability.
• Since the production methods of the mini tablets are easier, the tablets which have uniform size and dosage and do not differ from batch to batch can be produced.
• Superiority to granules
• Mini tablets have a smooth surface, stable surface area and high mechanical resistance compared to granules. It can be easily coated and requires less coating material than granules.

Formulation options of mini tablet dosage forms [12]

• Compressed mini tablets
• Encapsulated mini tablets
• Biphasic drug delivery system prepared as mini tablet

Mini tablets are usually used by filling with capsules or by tableting (Figure 1).

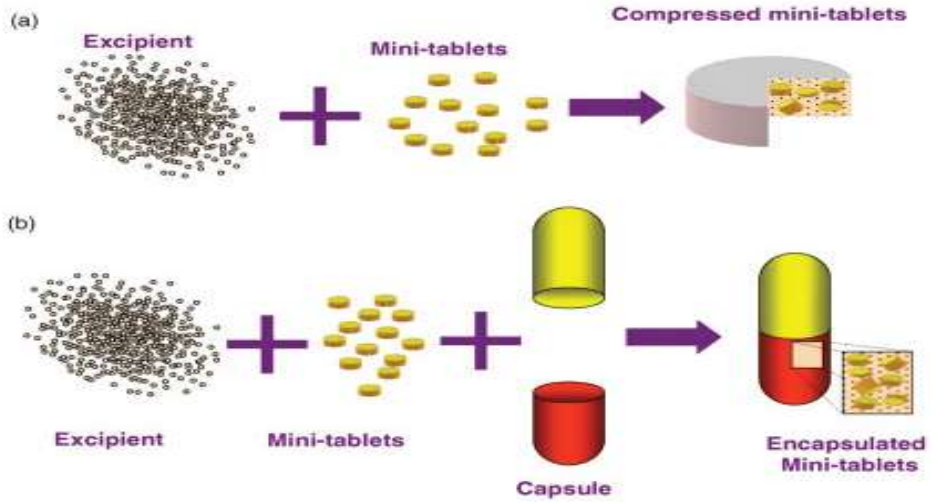

Figure 1: Tablet in capsule dosage form

Biphasic mini tablet

A biphasic mini tablet comprises two parts a fast releasing part and a slow-releasing part. The intention of biphasic delivery systems is to release drug at two different rates or at two different time periods: They are either quick/slow or slow/quick. A quick/slow-release system provides an initial burst of drug release followed in a controlled way of release over a defined period of time and in slow/quick release system provides release vice-versa. This type can helpful for drugs used in hypertension where repetitive dosing can be reduced. Different drugs can compact into mini tablets and filled in the same capsules to treat various diseases [13 , 14].

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Capsules as a carrier for Multiple Unit Drug Delivery Systems for Controlled Release:

MUDFs are mainly oral dosage forms consisting of a multiplicity of small discrete units, each exhibiting some desired characteristics. In these systems, the dosage of the drug substances is divided on a plurality of subunit, typically consisting of thousands of spherical particles with diameter of 0.05-2.00 mm. To deliver the recommended total dose, these subunits are filled into a capsule [15, 16].

Hard gelatin capsules are particularly suitable for their development and manufacture. Multiple-units might consist of a single pellet, or homogeneous granules, or a combination of several pellets and granules with various substances and different release characteristics. It is even possible to include a number of dosage forms – such as tablets, pellets, capsules, powders and granules – within a single formulation. In this way, incompatibilities and interaction between the different drug substances in combination products can be prevented [17].

This capsule design allows the filling of different types of MUDFs formulations such as powder-filled-capsules, granules-filled-capsules, beads-filled-capsule, tablets-filled capsule, caplets-filled- capsule and capsule-filled-capsule. Hard gelatin capsules therefore offer a highly flexible solution for MUDFs [18 – 20].

Mini tablets-in-a-capsule technology:

Controlled release capsules often containing plurality of coated pellets is yet another category of solid oral formulation that offers analogous therapeutic benefits. A relatively more recent approach that has come into existence is the one that combines the features of both controlled release tablets and modified release capsules in one dosage form [21]**.**

Drugs are usually encapsulated in one way or another within a barrier material, which is composed of an erodible or biodegradable polymer. Depending on the barrier material structure and thickness, different release lag times can be achieved. After the barrier material is dissolved, eroded or degraded, drugs are rapidly released from the inner reservoir core. Based on the concept that a formulation given once a time daily, a multifunctional and multiple unit system for oral use can be developed by filling versatile tablets in a hard capsule. This can be developed by preparing Rapid-release Mini-Tablets (RMTs), Sustained release Mini-Tablets (SMTs), Pulsatile Mini-Tablets (PMTs), and Delayed-onset Sustained-release Mini-Tablets (DSMTs), each with various lag times of release. Based on the combinations of mini-tablets, multiplied pulsatile drug delivery system (DDS), site-specific DDS, slow/quick DDS, quick/slow DDS, and zero-order DDS could be obtained. This system can be used for achieving the selective delivery of drugs at appropriate time, which is a chronopharmaceutical approach for the better treatment of disease with circadian rhythms. This novel system is a so called "mini-tablets-in-a-capsule technology". The designed capsule device consists of an impermeable capsule body and a soluble cap. The multi-layered tablets formulation prepared is filled within the capsule body and sealed with the water-soluble cap [22 – 26].

In this technology we can reduce the size of the tablet such that it could be enclosed in a capsule, and then deploy tablets with different release properties, within one single dosage form. This technology may be achieved by fast/slow delivery system. The proposed fast/slow delivery devices show a wide flexibility in the modulation of the delivery program. The two different release phases can be easily adjusted in a wide range of values of both delivery rate and ratio of the dose fractions, on the basis of the pharmacokinetics and therapeutic needs, to perform the desired in-vivo profile [27, 28].

Advantages of tablets-in-a-capsule technology:

1. It causes significant savings, lower treatment failure rate and lower case-fatality ratios.
2. Provides both controlled and multi-phase release for single or combination prescription and over the counter medicines.
3. Patient convenience and compliance and cost effective therapy can be achieved.
4. Delivering of incompatible APIs are possible.
5. Sustained, pulsed or delayed release profiles can be achieved.
6. Drug delivery can be targeted to two different regions of the GI tract.
7. It has higher colonic residence time, more predictable gastric emptying and consequently less money needed for the development of new products in long-term therapy.
8. It offers high drug loading, a wide range of release rate designs, and fine tuning of these release rates. It has less risk of dose dumping, less inter- and intra- subject variability, high degree of dispersion in the digestive tract thus minimizing the risks of high local drug concentrations. Broad therapeutic applications can be achieved. [21, 28]

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II. CONCLUSION

Mini – tablets offers various advantages over single unit dosage forms in terms of accuracy, feasibility, economy, novel research and targeted drug delivery system. Through the novel tablet in capsule delivery system, the formulator was able to achieve the biphasic delivery system of similar or different drugs. While we can modify the design of mini – tablets as per our objective of the study, we were able to release the drug at desired rate and pattern. They increase patient compliance by allowing coexistence of drugs with each other and by combining drugs with different release kinetics. Especially in geriatric and pediatric patient groups, there is a very high potential for achieving success in treatment. Hence tablet in capsule technique appears to be promising approach for delivery of two drugs in combination and as a once a day formulation dosage form with better patient compliance and therapeutic efficacy. Further research studies had to be undergone on tablet in capsule dosage form for treatment of various symptoms and their different combination of drugs.

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